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(54) **A method and apparatus for volumetrically controlled and reproducible introduction of small amounts of liquid samples into chromatographic analysis systems.**

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Description

The present invention relates to a method and an apparatus to perform sampling in chr matographic syst ms with very small amounts of liquid sample, said method and said apparatus being particularly even if not exclusively applicable to high resolution gas chromatographic systems, with capillary or micropacked columns, or to thin-layer chromatographic systems; this method and apparatus allow to perform controllable and reproducible sampling of very small amounts of sample, with values unattainable through the technique usually employed for liquid sampling in chromatographic systems and particularly using micro-syringes or pipettes.

The microsyringes used in chromatography are generally of the type with calibrated body (capable of sampling amounts ranging from 0.2 to 10 microliters) or of the type with calibrated needle, where the piston penetrates into the needle. The latter microsyringes are capable of handling smaller quantities of samples, in a reliable and reproducible way, but only within certain limits, in particular with lower limits of about 200—300 nanoliters. Below this limit, the high surface tension of the liquid and the relatively reduced speed of the piston movement do not allow the drop, which has formed at the needle end, to fall from it, considering the reduced diameter of the outlet nozzle of the needle. Precision is moreover negatively affected by poor sealing between piston and calibrated needle.

Another known system is the sampling system commonly used in laboratory and named "pipette system", in which a calibrated tubing is filled with a liquid to be transferred, by sucking it into the tubing, the liquid amount placed in the tubing is controlled and the same is retained in the tubing by closing same at the end where aspiration has been carried out. Then, an injection of the liquid into a receiving container is made by opening said end. This sampling method or transfer method of determined amounts of liquid is well known and has been used in gas chromatography too, but however only for quantities usually measurable in a rather rough way, even if the literature reports a lower limit of 25—50 nanoliters (see R. Kaiser—Gas Phase Chromatography—Vol. I pp. 90—95—Butterworths 1963—London).

Therefore it can be considered that, of course according to the nature of the liquid substance to be sampled, a lower limit exists, generally between 50 and 200 nanoliters, below which it is not possible to go in reliable and reproducible sampling using microsyringes or micropipettes.

Furtherm re, in the case of th pipett s, and also ften in th cas f the micr syring s, when the gaseous fluid betw en the piston and the sample liquid is not completely liminated, considering that quantitativ determination is performed during feeding, it may occur that the gas pushing the liquid out of the pipette, enters the capillary column, which sometimes involves problems connected with the choice and the us f said gas, such that it d es not aff ct analys s.

The ab ve mentioned quantitativ limitati ns, however, are such that the operator is often forced to perform accessory operations imposed by the relatively high quantities of sample that has to be introduced into the chromatographic system and particularly into the capillary column. In fact, specially in the case of direct injection without vaporization (on-column), particularly considered herein, the sample must be diluted in a dilution ratio which is often very high (of the order of 1:10000 or more), with an operation which may involve difficulties in the exact analytical determination of the sample and in that it can introduce discriminations or variations in the sample original conditions. In other cases, a so-called "splitting" operation is necessary, that means the elimination of a high percentage of the quantity fed to the injector, before its introduction into the column, which operation may involve even higher risks of discriminations.

Among the prior art documents the following can be cited: US—A—3988921 US—A—3475964 US—A—3479880 and GB—A—1172892. In particular GB—A—1172892 relates to a method and apparatus for dispensing liquid by gas pressure, wherein a liquid dispenser comprises a sample compartment within a first chamber, the sample compartment being provided with a delivery outlet and being adapted to receive liquid from a second chamber and to be filled to a pre-determined level therewith and a conduit being provided for returning to the second chamber liquid overflowed from the sample compartment, and the said first chamber being adapted to allow the establishment therein of a gas pressure whereby liquid is dispensed from the sample compartment.

According to this document the sample compartment defines the amount of liquid dispensed, and such amount cannot be controlled. Further, this method and apparatus do not allow dispensing very small liquid amounts.

Accordingly, an object of the invention is to provide a method and an apparatus allowing to perform sampling in chromatographic system with very small amounts of liquid sample, especially quantities from 10 picoliters to 50 nanoliters; in a reproducible way under the same sampling conditions and sample type.

Another object of the present invention is to provide a method and apparatus as above said in which the introduction of said small or very small amounts of liquid sample does not require the parallel introduction into the chromatographic system of another substance, either a liquid or gaseous one, to propel the sample out of th sampling container.

Still an ther object f the pr sent invention is t provide a m th d and apparatus as above said and operating under the specified conditions, wh rein the volumetric dosage of the substance

injected into the chromatographic system is performed with the maximum of reliability, precision and reproducibility, during the injection stage itself.

According to the inv ntion a method is provided for sampling with very small quantities f liquid sample, especially from 10 picolitres to 50 nanolitres in chromatographic systems, especially in high-resolution gas chromatographic or thin-layer chromatographic systems, said method comprising the following steps:

— taking a sample container having a higher volume than the quantity to be sampled
— filling said container with a sample quantity
— introducing, before or after filling thereof, said container or part of same into an injector or a device for sample injection into the chromatographic system;
— submitting the liquid inside the container to a given pressure, characterized in that it further comprises the following steps:

a) taking a sample container having a pipette or nozzle-shaped neck acting as outlet, with maximum size ranging between 1 and 100 µm, preferably between 1 and 30 µm;

b) filling said container with a sample quantity greater than the one to be sampled and controlling that, in correspondence with said outlet opening, a meniscus of the sample liquid is formed;

c) submitting the liquid inside the container to at least one pressure pulse having a pressure value sufficient to overcome the surface tension of the liquid sample in correspondence with the outlet and a duration limited in time according to said pressure value and to the quantity to be sampled, keeping into consideration the outlet opening size, the pressure pulse amplitude, the sample characteristics and the number of pulses;

d) abruptly reducing the pulse pressure down to a value lower than the one sufficient to overcome the surface tension of the liquid in correspondence with the outlet opening of the container.

Therefore, according to said method, it is now possible to carry out sampling of extremely reduced quantities of liquid, using a container which can be of the substantially traditional type, except for the outlet neck, to which a device can be applied which allows to create said pressure pulse, in such a way that the sample drawing and eventual washing of the container can be performed with extremely simple and traditional systems and means, though being possible to perform said samplings with extremely reduced quantities.

Considering the performance of the system according to the invention, in most cases, the sample can be injected directly into the column, without vap rization. Vaporization may become necessary nly in case of so-called "dirty" sampl s to prevent substances with high m lecular weight contained in said samples fr m being directly introduced into the capillary column.

Said method according to the invention can be substantially performed according to two different ways, the first of which considers the applicati n of a pneumatic pulse, obtained by operating for time periods of the order of milliseconds an electrovalve which allows to exert a pressure in correspondence with a gaseous element directly or indirectly placed in contact with the sample in the container, while the second one considers the application, to the container body and/or to means mechanically connected with the same, of a mechanical pulse, obtained with a piezoelectric system a magnetostrictive system or other similar one, which determines an extremely high and extremely quick pressure increase in the liquid.

As previously said, the invention relates also to an apparatus for volumetrically controlled and reproducible injection of very small quantities of liquid sample, especially from 10 to picolitres to 50 nanolitres into chromatographic systems, especially into high-resolution gas chromatographic or thin layer chromatographic systems, and comprising:

— a sample container having a volume greater than the liquid quantity to be sampled
— means to operatively position said container in a sample injection device of a chromatographic system, for injection of sample through said outlet opening; and means to submit the liquid inside the container to a pressure, characterized in that said sample container has a pipette or nozzle-shaped outlet opening, with a maximum size ranging between 1 and 100 µm, preferably between 1 and 30 µm; and in that said means to submit the liquid to a pressure are means to submit the liquid inside the container to at least one pressure pulse controlled in amplitude and or duration.

In the annexed drawings:

Figure 1 is an enlarged view, in axial section, showing possible shapes of the outlets of containers for samples to be used according to the invention.

Figures 2 and 3 are examples of possible pressure pulses used in the method and equipment according to the invention to perform desired sampling.

Figure 4 is a diagrammatic view, with parts in section, of an equipment for performing sampling by the use of pneumatic pulses.

Figures 5 and 6 diagrammatically show embodiments of equipments for sampling by means of pressure pulses obtained with a piezoelectric system and magnetostrictive system, respectively.

Figur 7 is a diagrammatic view showing possible reciprocal positions of container outlets, in one of the equipments pr viously illustrated, and the end of a capillary column in applications

to high resolution gas chromatography with capillary columns.

Figures 8 and 9 are diagrammatic views of other possible positions f the sample c ntain r and of the end of the capillary column for the same uses as consider d in Figure 7.

The invention relates, as already said, to a method and an apparatus for sampling, in chromatographic systems, of liquid samples, said method and said apparatus being particularly applicable to laboratory chromatographic systems, specially in high resolution gas chromatography with capillary columns and with direct on-column injection of the sample, without previous vaporization, or to thin-layer chromatographic systems. In particular, chromatographic systems of the direct injection type are well known and applied, wherein the liquid sample is injected directly into the initial part of the column and then is moved along the latter by means of a carrier gas, the sample being simultaneously vaporized. The method and apparatus according to the invention are capable, specially in chromatographic systems of the above mentioned type, of allowing injection of a quantity of liquid sample so reduced in volume that all this quantity can be analyzed in the chromatographic system, without any need of dilution as necessary in traditional methods and equipments to obtain a precise dosage of the injected sample. Though greater amounts can also be injected, the method and apparatus which will be illustrated are particularly suitable for the injection in a reliable and reproducible way, of liquid samples in quantities ranging between 10 picoliters and 50 nanoliters, namely amounts so small which cannot be taken into consideration with the previously employed systems.

The method and the apparatus of the invention are based on the use of a container for the liquid sample, which has a volume greater than that of the sample to be analyzed, said container being made of any suitable material, for instance glass, metal, fused silica or any other material, and having a pipette shape, a syringe needle shape or any other suitable shape.

The essential condition is that said container, as indicated by 10 or 12 in Figure 1, presents a neck defining an outlet having a maximum size (a diameter *d* in this specific case) ranging from 1 to 100 µm, preferably between 1 and 30 µm. Said neck can be nozzle-shaped, as indicated by 14 in Figure 1, and therefore has a preferred neck diameter *d* from 10 to 30 µm, or micropipette-shaped, as indicated by 16 in the same Figure 1, with a preferred diameter *d* from 1 to 20 µm. The container, 10 or 12 as illustrated in Figure 1, can be filled with usual methods, for instance by means of a syringe, by gravity, by capillarity or in any way whatsoever, with a quantity of liquid 18 which is greater than the volum that is required to flow from the neck 14 or 16 to be analyzed in th chromatographic system. Once th container 10 or 12 has been fed with the sample 18, it is necessary to check, specially in the case of th container 12 with pipette-like end, that the liquid goes as far as to reach the neck 14 or 16, forming a meniscus therein. Under these conditions, taking into account the reduced siz of the neck, the surface tension of the liquid prevents the latter from flowing out of the neck, forming drops, this obviously provided that the neck 14 or 16 does not touch foreign bodies, as for instance the wall of the gas chromatographic column, which may help the liquid to flow outside the column. Once the feeding of the container 10 or 12 as previously indicated has been carried out, for ejecting a measured amount of liquid 18 through the neck 14 or 16, pressure on the liquid 18 is exerted directly or indirectly as schematically shown by the arrows 20 in Figure 1. Said pressure is controlled in amplitude and in time as indicated in Figures 2 and 3, keeping into consideration that the liquid amount ejected depends both on the amplitude, namely the value of the pulse pressure, on the duration of the pulse itself and on the number of pulses.

As it can be seen from Figures 2 and 3, the pulse has a step configuration and it is very important that the downwards section of same, namely pressure return to zero, be placed vertically as much as possible in order to avoid during this stage, in correspondence to the neck 14 or 16, the formation of a drop which will remain in position, thus completely altering any measuring of the injected sample. In the case of Figure 2, the pressure pulse is a pneumatic pulse and reaches a value p_1 which must be in any case higher than the one necessary to overcome the surface tension of the liquid in correspondence with the neck 14 or 16. In relation to the pressure value p_1, the duration Δt of the pulse is chosen, variable from about a millisecond to about a second, in order to obtain the desired quantities of ejected liquid.

The pressure values can range from 1 to 10 atmospheres. Alternatively, it can obviously be possible to emit several pulses having lower duration. However, for an exact reproducibility of sampling, it is very important to reduce to the minimum the dead space, that is the gas volume on which each pressure pulse acts.

The situation illustrated in Figure 3 is the one that occurs in case of a pressure pulse exerted by means of magnetostriction, or piezoelectricity. In this case, the time Δt is extremely reduced and corresponds to the resonance frequence of the laminations forming the magnetostriction device or to the frequence of the piezoelectric material, ranging from 10 to 100 KHZ, while a certain regulation of the quantity emitted at each pulse can be performed by varying the amplitude of the electric pulse given to the device and consequently the pulse pressure value given to the liquid, said pressure value being in any case of ne or s veral ord rs higher than that nec ssary in the pn umatic case. An apparatus for carrying-out th meth d according to th inventi n with pneumatic pulse is diagrammatically illustrated in Figur 4, wherein a receiv r 10 of th type

illustrated in the left side of Figure 1 is provided, which has preferably a very small inner diameter and which can be removably fixed, for example by means of a locking nut 22 and a gasket 24 compressed by said nut, in a supporting block 26 which presents a groove 28 for feeding gas under pressure, for instance air. The block 26 can present another groove 30 which can be closed by a locking element 32 to feed the container 10 with the sample 18. The locking element comprises a protrusion 33, for example in metal, to reduce to the minimum the dead space.

The duct 28 is connected, in any known way, to a circuit for supply air under pressure coming from a source 34, said circuit comprising a pressure regulator 36 and an electrovalve 38, the opening time of which can be regulated by means of a device 40, known in itself. A duct 42 is positioned between the electrovalve 38 and block 26 and advantageously presents a very small inner size, in such a way to reduce to the minimum the so-called dead volume, that is the volume of air comprised between the valve 38 and the upper meniscus of liquid 18 within the container 10. Said reduction of the dead volume is very important to obtain a quick fall of pressure at the end of the pulse and then to be sure that no drop forms and remains in correspondence to the container 10 outlet.

The apparatus of Figure 4 can be fed through the opening 32 for instance by means of a usual syringe, with a sample quantity much greater than the one which must be used for injection into the gas chromatographic system. Once the feeding is performed, the opening 32 is closed, the container is introduced into the chromatographic system and the valve 38 is opened for a time period controlled by the device 40, in such a way as to create a pressure pulse having a value regulated by the element 36. In this way, a small jet of liquid forms and breaks out in small drops in a point which is the farther from the outlet neck 14 the highest is the pressure value set in regulator 36, of course with same type of liquid and same size of neck.

The sampling device illustrated in Fig. 5 operates with a piezoelectric system which, in its part including the element for formation and emission of the jet of drops, is substantially featured like a ink-drops printing device, of the "jet on demand" type, known in itself. It essentially comprises a container 44, for example but not necessarily with a cylindric shape, made of glass or fused silica, ready to be filled in its lower section with the sample to be injected into the column for instance introduced through the upper section thereof.

The container 44 ends in its lower section with a calibrated nozzle 14, as previously indicated, through which the liquid jet of sample is emitted. Under atmospheric pressure conditions, the liquid does not flow out of the nozzle 14 because of its surface tension.

The container 44 is connected to a transducer 50 of piezoelectric type, capable of provoking, when excited, a sudden volume variation inside the container 44 and therefore a sudden pressure variation in the liquid present in it, such as to determine the flowing out of a calibrated jet of one or more drops through the nozzle 14. The transducer 50, which is placed very near to the nozzle 14 and housed for example in a small block 52 made of plastic material, is excited by means of a source of electrical pulses 54, which have the characteristics previously described, feeding of the transducer 50 on its electrodes 51, through a circuit 53 having a switch 55 by means of which the operator can close the circuit and then control the emission of the jet of drops. To the source 54 a known means 56 is connected to vary the amplitude of pulse or pulses communicated to the transducer 50; another component 57 is also connected, capable of controlling the duration of the pulse or series of pulses.

For operation, the container 44 must be filled with the liquid sample, possibly by means of a microsyringe, at least in its section close to the nozzle 14, and the transducer 50 is submitted to a pulse or series of pulses having a predetermined amplitude, during which, in correspondence with the nozzle 14, a jet of one or more drops of sample liquid is emitted, in a small pre-settable quantity. Said jet presents high directionality and an extremely limited increase in diameter, so that it can be directed into column with one of the systems which will be considered, for example through the injection port of a direct injector, equipped with a "slice" type or rotative valve.

The amplitude of pulses may be regulated by the element 56, in order to obtain a corresponding regulation of the pressure increase provoked by said pulses and consequently of a first parameter affecting the operative conditions, in particular of the correct formation of the jet of drops, considering the nozzle diameter and the nature of the treated liquid. When the other conditions are kept unchanged, the ejected quantity of a given sample, thanks to the formation of a pulse having a preset amplitude, is exactly definite and equal to a drop, and therefore the ejected quantity obtained by a series of pulses will depend only on the duration of the latter and therefore on the number of pulses forming such series, because the time period of each pulse is determined by the transducer characteristics.

The apparatus illustrated in Figure 6 consists of a container 44 having a needle-syringe shape 46 with piston 48. The needle 44 is introduced into a duct 58 inside the body of an injector 60, of a type known in itself and provided with a valve 62, said injector body being provided with a magnetostriction apparatus 64, acting on the needle 44, which is made of nickel. The exerted pressure is sufficient for determining a sample ejection, in the desired quantity, independently from the position of the syringe piston 48, obviously provided that the liquid 18 fills the container 44 at least partly and as far as the outlet neck 14. Both in the case of a pneumatic-type pulse and in the case of a mechanic-type pulse, such as a pi zo-

electric or magnetostrictiv one, when the method and th equipment according to th invention are applied to a high-resoluti n gas chr mat graphic system with capillary column, it is possible to have two cases of a reciprocal disp sition of c ntainer 10 or 12 and capillary column 66, the first one of these cases being indicated in Figure 7. According to said figure, the container 10 or 12 shows an outer diameter which is smaller than the inner diameter of the capillary column 66 or of an enlarged end 67 of same, and is therefore inserted into the injector as far as to penetrate with its end section into the inlet opening of the capillary column 66. In this case, the emission of liquid sample under the stated conditions is only conditioned by the fact that the neck 14 does not touch any component and in particular the column 66 wall. Both during sample injection and after this operation, a current of carrier gas is present, which penetrates into the column through the hollow space existing between the column wall and container 10, as indicated by arrows 68.

On the contrary, the case in which the capillary column has an inner diameter smaller or equal to the outer diameter of container 10 or 12 is illustrated, for the two types of container, in Figures 8 and 9. In this case, the injector body 70 shows a neck 72, which advantageously has an axial length as small as possible and on the two sides of which there are positioned the column 66 and the container 10 or 12, the latter being preferably housed in a protecting element 74, which provides for leaning the seat of said container 10 or 12 on the walls. In this case, it is advisable, as already said, (i) that the distance between the outlet neck 14 or 16 of container 10 or 12 and the column 66, as measured in an axial direction, be as small as possible, for instance 10 mm maximum, (ii) that the injection pressure of the jet into the neck 14 or 16 be sufficient for maintaining the latter in such a condition as to give rise to a very small opening angle of the jet, and (iii) that the axial alignment of the neck 14 and column 66 be perfect. It is particularly important in this case that, during injection, the carrier feeding, always according to arrows 68, be discontinued to avoid that the carrier gas drags outside part of the injected sample, especially if the latter contains easily vaporizable substances.

The system according to the invention, herein described as an example, has proved to be very useful in particular for capillary columns with very small diameters, according the present trend in this field.

Finally, it should also be noticed that the embodiments of the present invention as above illustrated and described can be submitted to several changes and variations without departing from the spirit and scope of the invention as claimed, thes variations comprising th one c nsidering an automatic sampl r, wher in th c ntainer is aut matically filled and wh rein sample emission occurs through several jets of sample.

Claims

1. A method for sampling with very small quantities of liquid sampl , especially from 10 picoliters to 50 nanolit rs in chromatographic systems, especially in high resolution gas chromatographic or thin-layer chromatographic systems, said method comprising the following steps:

— taking a sample container having a higher volume than the quantity to be sampled;
— filling said container with a sample quantity;
— introducing, before or after filling thereof, said container or part of same into an injector or a device for sample injection in to the chromatographic system;
— submitting the liquid inside the container to a given pressure, characterized in that it further comprises the following steps:

a) taking a sample container (10, 12) having a pipette or nozzle shaped neck (14, 16) acting as outlet, with maximum size ranging between 1 and 100 µm, preferably between 1 and 30 µm;

b) filling said container with a sample quantity greater than the one to be sampled and controlling that, in correspondence with said outlet opening, a meniscus of the sample liquid (18) is formed;

c) submitting the liquid inside the container to at least one pressure pulse having a pressure value sufficient to overcome the surface tension of the liquid sample in correspondence with the outlet and a duration limited in time according to said pressure value and to the quantity to be sampled, keeping into consideration the outlet opening size, the pressure pulse amplitude, the sample characteristics and the number of pulses;

d) abruptly reducing the pulse pressure down to a value lower than the one sufficient to overcome the surface tension of the liquid in correspondence with the outlet opening of the container.

2. A method according to claim 1, characterized by the following steps:

— providing a sample container (10) presenting a zone of small volume, opposite to the outlet opening and usually not filled with liquid;
— connecting said zone of the sample container to a source (34) of gas under pressure, through a control valve (38) and a duct (42), said duct having, between the valve and container, a small volume;
— controlling the values of pressure supplied and/or opening time of the valve (38) necessary to form said pressure pulse.

3. A meth d according to claim 2, characterized in that pressures ranging from 1 t 10 atmospheres and valve opening times fr m 1 millisecond to 1 second are used.

4. A method according t claim 1, characteriz d

in that each pressure pulse is obtained by magnetostriction or by piezoelectric means.

5. A method according to claim 4, characterized in that at least part of said container (44), in the zone thereof containing the liquid sample, cooperates with a piezoelectric transducer (50) and wherein said transducer is submitted to at least one electric pulse to give rise to a corresponding pressure pulse in the liquid inside the container (44).

6. A method according to claim 4, characterized in that at least part of said container (44), in the zone thereof containing the liquid sample, is made of nickel; in that a control apparatus (64) with magnetostrictive actuation is provided in the sample injector or injection device, in such a way as to cooperate with the nickel part of said container, when the latter is in operative position, and wherein said apparatus (64) is submitted to at least one current pulse having an adjustable amplitude to give rise to a corresponding pressure pulse in the liquid contained in the nickel part of the container (44).

7. An apparatus for volumetrically controlled and reproducible injection of very small quantities of liquid sample, especially from 10 picolitres to 50 nanolitres into chromatographic systems, especially into high-resolution gas chromatographic or thin-layer chromatographic systems, and comprising:

— a sample container having a volume greater than the liquid quantity to be sampled;
— means to operatively position said container in a sample injection device of a chromatographic system, for injection of sample through said outlet opening; and
— means to submit the liquid inside the container to a pressure, characterized in that said sample container (10, 12) has a pipette or nozzle-shaped outlet opening (14, 16), with a maximum size ranging between 1 and 100 µm, preferably between 1 and 30 µm; and in that said means to submit the liquid to a pressure are means to submit the liquid inside the container to at least one pressure pulse controlled in amplitude and/or duration.

8. An apparatus according to claim 7, characterized in that it comprises means for pneumatic connection between said container (10), on the side thereof opposite to the outlet opening, and a source (34) of gas under pressure, said connecting means comprising a control valve (38) and one or more ducts (42) connecting said valve to the container, said duct or ducts being sized in such a way as to reduce as much as possible the gaseous volume between the sample liquid in the container (10) and the control valve (38).

9. An apparatus according to claim 8, characterized by means (36) to adjust pressure between 1 and 10 atmospheres and means (40) to control the opening time of the valve between 1 millisecond and 1 second.

10. An apparatus according to claim 7, characterized in that said means to submit the liquid to one or more pressure pulses comprise: at least a transducer (50, 64) capable of producing one or more pressure pulses, at high pressure value and short duration, in the sample container (44); a pulse source (54) to excite said transducer and means (56, 57) to adjust the amplitude of pulses and/or the number of them.

11. An apparatus according to claim 10, characterized in that said transducer is a piezoelectric transducer (50) and said pulse source (54) is a source of electric pulses of high steepness.

12. An apparatus according to claim 11, characterized in that said container (44) is made of glass or fused silica and is surrounded, near to the outlet opening thereof, by a piezoelectric transducer (50) plunged in a small block (52) of a plastic material.

13. An apparatus according to claim 10, characterized in that the container (44) has at least a section made of nickel in the zone containing the liquid sample; wherein the transducer is formed by a magnetostrictive apparatus (64) capable of acting on said container section when in its operative position within a seat provided in said magnetostrictive apparatus, and wherein said apparatus comprises receiving means of at least one current pulse having an adjustable amplitude, to give rise to a pressure pulse in said container nickel section.

14. An apparatus according to claim 13, characterized in that said pulse has a duration depending on the frequency of mechanical resonance of the magnetostrictive apparatus and is adjustable in amplitude.

15. The use of an apparatus according to one of the claims from 7 to 14, in high-resolution gas chromatographic systems with a capillary column, characterized in that said container (10, 12) has at least an end section having a maximum size smaller than the inner diameter of said capillary column where chromatographic separation occurs, and in that said gas chromatographic system has an on-column type injector with means to axially control the container position so that its end section penetrates into the column inlet opening.

16. The use of an apparatus according to at least one of claims 7 to 14, in high-resolution gas chromatographic systems with a capillary column, characterized in that said chromatographic system has an injector (70) presenting a device for reciprocal alignment and axial centering of the chromatographic column inlet end (66) and of the container outlet end (10, 72) in an axially spaced position up to a distance not exceeding 10 mm.

17. The use according to claim 16, characterized in that said chromatographic system has means to discontinue carrier gas feeding during injection.

18. The use according to claim 16 or 17, characterized in that at least an external protection element (74) is associated to the container end section.

Patentansprüche

1. Verfahren zur Probenentnahme mit sehr geringen flüssigen Probenmengen, insbesondere von 10 Pik liter bis 50 Nan liter in chromatographischen Systemen, bes nders in gaschromatographischen Hochauflösungs- oder dünnschichtchromatographischen Systemen, wobei dieses Verfahren die folgenden Stufen umfasst:

— Nehmen einen Probenbehälters, der ein grösseres Volumen als die zu probierende Menge hat;
— Füllen diese Behälters mit einer Probenmenge;
— Einführen diese Behälters oder eines Teiles davon, vor oder nach dessen Füllung, in einen Injektor oder in eine Vorrichtung für Probeninjektion in das chromatographische System;
— Aussetzen der Flüssigkeit im Behälter einem gegebenen Druck,

dadurch gekennzeichnet, dass dasselbe ferner die folgenden Stufen umfasst:

a) Nehmen eines Probenbehälters (10, 12) mit einem pipetten- oder düsenförmigen Hals (14, 16), der als Auslass dient, mit einer maximalen Grösse von 1 bis 100 µm, vorzugsweise von 1 bis 30 µm;
b) Füllen dieses Behälters mit einer grösseren Probenmenge als der zu probierenden, und Kontrollieren, dass sich an dieser Auslassöffnung ein Meniskus dieser Probenflüssigkeit (18) bildet;
c) Aussetzen der Flüssigkeit im Behälter wenigstens einem Druckimpuls mit einem Druckwert, welcher ausreicht, die Grenzflächenspannung der flüssigen Probe am Auslass zu überwinden, und von einer zeitmässig beschränkten Dauer gemäss diesem Druckwert und der zu probierenden Menge, unter Berücksichtigung der Auslassöffnungsgrösse, der Druckimpulsamplitude, der Probeneigenschaften und der Impulsanzahl;
d) plötzliches Verringern des Impulsdruckes auf einen geringeren Wert als den für die Überwindung der Grenzflächenspannung der Flüssigkeit an der Behälterauslassöffnung ausreichenden Wert.

2. Verfahren nach Anspruch 1, gekennzeichnet durch die folgenden Stufen:

— Nehmen eines Probenbehälters (10) mit einem kleinen Volumenbereich gegenüber der Auslassöffnung und normalerweise nicht mit Flüssigkeit gefüllt;
— Verbinden dieses Probenbehälterbereiches mit einer unter Druck stehenden Gasquelle (34) über ein Steuerventil (38) und einen Kanal (42), wobei dieser Kanal zwischen Ventil und B hälter in kleines V lumen aufweist;
— Einst llen der gelieferten Druckwerte und/oder der zur Bildung dieses Druckimpulses nötigen Öffnungszeit des Ventils (38).

3. Verfahren nach Anspruch 2, dadurch gek nnzeichnet, dass Drucke von 1 bis 10 Atmosphären und Ventilöffnungszeiten v n 1 Millis k. bis 1 Sek. verwendet werden.

4. Verfahren nach Anspruch 1, dadurch gekennzeichnet, dass jeder Druckimpuls durch magnetostriktive oder piezoelektrische Mittel erhalten wird.

5. Verfahren nach Anspruch 4, dadurch gekennzeichnet, dass wenigstens ein Teil dieses Behälters (44), in seinem die flüssige Probe enthaltenden Bereich, mit einem piezoelektrischen Umformer (50) zusammenarbeitet, und dass dieser Umformer wenigstens einem elektrischen Impuls ausgesetzt wird, um einen entsprechenden Druckimpuls in der Flüssigkeit im Behälter (44) zu erzeugen.

6. Verfahren nach Anspruch 4, dadurch gekennzeichnet, dass wenigstens ein Teil des genannten Behälters (44), in dessen die flüssige Probe enthaltenden Bereich aus Nickel hergestellt ist, dass ein Steuergerät (54) mit magnetostriktiver Betätigung im Probeninjektor oder in der Injektionsvorrichtung in der Weise vorgesehen ist, dass dieses mit dem Nickelteil des genannten Behälters zusammenarbeitet wenn letzterer sich in wirksamer Stellung befindet, und dass dieses Gerät (64) wenigstens einem Stromimpuls mit einer einstellbaren Amplitude ausgesetzt wird, um einen entsprechenden Druckimpuls in der im Nickelteil des Behälters (44) enthaltenen Flüssigkeit zu erzeugen.

7. Gerät zur reproduzierbaren und volumetrisch kontrollierten Injektion von sehr geringen flüssigen Probenmengen, insbesondere von 10 Pikoliter bis 50 Nanoliter, in chromatographischen Systemen, besonders in gaschromatographischen Hochauflösungssystemen oder dünnschichtchromatographischen Systemen, und umfassend:

— einen Probenbehälter mit einem grösseren Volumen als die zu probierende flüssige Menge;
— Mittel zum operativen Positionieren dieses Behälters in einer Probeninjektionsvorrichtung eines chromatographischen Systems zur Probeninjektion durch diese Auslassöffnung; und
— Mittel zum Aussetzen der Flüssigkeit im Behälter einem Druck,

dadurch gekennzeichnet, dass dieser Probenbehälter (10, 12) eine pipetten- oder düsenförmige Auslassöffnung (14, 16) aufweist, mit einer maximalen Grösse von 1 bis 100 µm, vorzugsweise von 1 bis 30 µm, und dass dieses Mittel zur Druckaussetzung der Flüssigkeit Mittel sind, um die Flüssigkeit im Behälter wenigstens einem in Amplitude und/oder Dauer kontrollierten Druckimpuls auszusetzen.

8. Gerät nach Anspruch 7, dadurch gek nnzeichnet, dass dasselbe Mittel zur pneumatischen V rbindung zwisch n dies m Behält r (10) auf dessen der Auslass ffnung gegenüberliegenden

Seite und einer Quelle (34) für unter Druck stehendem Gas aufweist, wobei dieses Verbindungsmittel ein Steuerventil (38) und einen oder mehrere Kanäle (42), die dieses Ventil mit dem Behälter verbinden, umfasst, wobei dieser Kanal oder diese Kanäle derart bemessen sind, dass das Gasvolumen zwischen Probenflüssigkeit im Behälter (10) und Steuerventil (38) so weit wie möglich reduziert wird.

9. Gerät nach Anspruch 8, gekennzeichnet durch Mittel (36) für die Druckeinstellung von 1 bis 10 Atmosphären, und durch Mittel (40) für die Einstellung der Offnungszeit des Ventils von 1 Millisek. bis 1 Sekunde.

10. Gerät nach Anspruch 7, dadurch gekennzeichnet, dass diese Mittel zum Aussetzen der Flüssigkeit einem oder mehreren Druckimpulsen wenigstens einen Umformer (50, 64), der einen oder mehrere Druckimpulse von hohem Druckwert und von kurzer Dauer im Probenbehälter (44) erzeugen kann, eine Impulsquelle (54) um diesen Umformer zu erregen und Mittel (56, 57) zum Einstellen der Impulsamplitude und/oder deren Anzahl, umfasst.

11. Gerät nach Anspruch 10, dadurch gekennzeichnet, dass dieser Umformer ein piezoelektrischer Umformer (50) ist, und die Impulsquelle (54) eine Quelle von elektrischen Impulsen großer Steilheit ist.

12. Gerät nach Anspruch 11, dadurch gekennzeichnet, dass dieser Behälter (44) aus Glas oder geschmolzener Kieselsäure hergestellt und in der Nähe dessen Auslassöffnung von einem in einem kleinen Kunststoffblock (52) eingebetteten piezoelektrischen Umformer (50) umgeben ist.

13. Gerät nach Anspruch 10, dadurch gekennzeichnet, dass der Behälter (44) wenigstens einen aus Nickel hergestellten Teil im die flüssige Probe enthaltenden Bereich hat, dass der Umformer durch ein magnetostriktives Gerät (64) gebildet ist, das auf diesen Behälterteil einwirken kann wenn er sich in seiner operativen Stellung in einem in diesem magnetostriktiven Gerät vorgesehenen Sitz befindet, und dass dieses Gerät Aufnahmemittel für wenigstens einen Stromimpuls mit einstellbarer Amplitude, um einen Druckimpuls in diesem Behälternickelteil zu erzeugen, umfasst.

14. Gerät nach Anspruch 13, dadurch gekennzeichnet, dass dieser Impuls eine Dauer in Abhängigkeit der mechanischen Resonanzfrequenz des magnetostriktiven Gerätes hat und in Amplitude einstellbar ist.

15. Verwendung eines Gerätes nach einem der Ansprüche 7—14, in gaschromatographischen Hochauflösungssystemen mit einer Kapillarsäule, dadurch gekennzeichnet, dass dieser Behälter (10, 12) wenigstens einen Endteil mit einer geringeren maximalen Grösse als der Innendurchmesser dieser Kapillarsäule, wo die chromatographische Trennung erfolgt, hat, und dass dieses gaschromatographische System einen on-column Injektortype mit Mitteln zum axialen Einstellen der Behälterpositi n hat, so dass sein Endteil in die Säuleneingangsöffnung indringt.

16. Verwendung eines Gerätes nach wenigstens einem der Ansprüche 7—14 in gaschromatographischen Hochauflösungssystemen mit einer Kapillarsäule, dadurch gekennzeichnet, dass dieses chromatographische System einen Injektor (70) mit einer Vorrichtung zum gegenseitigen Ausrichten und axialen Zentrieren des chromatographischen Säuleneinlassendes (66) und des Behälterauslassendes (10, 72), in einer Position, die sich in einem axialen Abstand von nicht mehr als 10 mm befindet, hat.

17. Verwendung nach Anspruch 16, dadurch gekennzeichnet, dass dieses chromatographische System Mittel zum Unterbrechen der Trägergaszuführung während der Injektion hat.

18. Verwendung nach Anspruch 16 oder 17, dadurch gekennzeichnet dass wenigstens ein äusseres Schutzelement (74) dem Behälterendteil zugeordnet ist.

Revendications

1. Procédé pour l'échantillonage avec des trés petites quantités d'échantillon liquid, en particulier de 10 picolitres à 50 nanolitres, dans des systèmes de chromatographie, spécialement dans des systems de chromatographie en phase gazeuse à haute résolution ou de chromatographie en couche mince, ledit procédé comprenant les phases suivantes:

— prendre un conteneur d'échantillons ayant un volume plus grande que la quantite à introduire;
— remplir ledit conteneur avec une quantité d'échantillon;
— introduire, avant ou après le remplissage, ledit conteneur ou une partie du même dans un injecteur ou un dispositif pour l'introduction d'échantillons dans le système de chromatographie;
— soumettre le liquide du conteneur à une pression préfixée, caractérisé en ce qu'il comprend aussi les phases suivantes:

a) prendre un conteneur d'échantillons (10, 12) ayant un col (14, 16) façonné en pipette ou en buse servant de sortie, avec une dimension maximale de 1 à 100 µm, préférablement entre 1 et 30 µm;

b) remplir ledit conteneur avec une quantité d'échantillon plus grande que la quantité à introduire et contrôler qu'à proximité de ladite sortie il y ait un ménisque de l'échantillon liquide (18);

c) soumettre le liquide dans le conteneur à au moins une impilsion de pression ayant une valeur suffisante pour vaincre la tension superficielle de l'échantillon liquide en correspondance de ladite sortie et une durée limite dans le temps selon ladite valeur de pression et la quantité à introduire, compte tenu des dimensions de l'ouverture de sortie, de l'amplitude de l'impulsion de pression, des caractéristiques de l'échantillon et du nombre des impulsions;

d) réduire brusquement la pression de l'impulsion jusqu'à une valeur inférieure à la valeur suffisante pour vaincre la tension superficielle du liquide en correspondance de l'ouverture de sortie du conteneur.

2. Procédé selon la revendication 1, caractérisé par les phases suivantes:

— disposer d'un conteneur d'échantillons (10) présentant une zone de volume réduit en opposition à l'ouverture de sortie et habituellement non remplie de liquide;
— relier ladite zone du conteneur d'échantillons à une source (34) de gaz sous pression, à travers une vanne de commande (38) et un conduit (42), ledit conduit ayant, entre la vanne et le conteneur, un volume réduit;
— contrôler les valeurs de la pression utilisée et/ou le temps d'ouverture de la vanne (38) nécessaires pour former ladite impulsion de pression.

3. Procédé selon la revendication 2, caractérisé en ce que les pressions utilisées varient de 1 à 10 atmosphères et les temps d'ouverture de la vanne de 1 milliseconde à 1 seconde.

4. Procédé selon la revendication 1, caractérisé en ce que chaque impulsion de pression est obtenue par magnétostriction ou par des moyens piézo-électriques.

5. Procédé selon la revendication 4, caractérisé en ce qu'au moins une partie dudit conteneur (44), dans la zone du même contenant l'échantillon liquide, coopère avec un transducteur piézo-électrique (50), et en ce que ledit transducteur est soumis à au moins une impulsion électrique pour provoquer une impulsion de pression correspondante dans le liquide présent dans le conteneur (44).

6. Procédé selon la revendication 4, caractérisé en ce qu'au moins une partie dudit conteneur (44), dans la zone du même contenant l'échantillon liquide, est faite de nickel; en ce qu'un appareil de commande (64) à actionnement magnétostrictif est prévu dans l'injecteur ou dans le dispositif d'injection, de sorte à coopérer avec la partie du conteneur en nickel lorsque ce dernier est dans sa position de travail, et en ce que ledit appareil (64) est soumis à au moins une impulsion de courant ayant une amplitude réglable pour donner lieu à une impulsion de pression correspondante dans le liquide contenu dans la partie en nickel du conteneur (44).

7. Appareil pour l'injection volumétriquement contrôlée et reproduisible de très petites quantités d'échantillon liquide, en particulier de 10 picolitres à 50 nanolitres, dans des systèmes de chromatographie, spécialement dans des systèmes de chromatographie en phase gazeuse à haute résolution ou de chromatographie en couche mince, et comprenant:

— un conteneur d'échantillons ayant un volume plus grand que la quantité de liquide à injecter;
— des moyens pour placer ledit conteneur en sa position de travail, dans un dispositif d'injection d'échantillons d'un système de chromatographie, pour l'injection de l'échantillon à travers ladite ouverture de sortie; et
— des moyens pour soumettre le liquide dans le conteneur à une pression, caractérisé en ce que ledit conteneur d'échantillons (10, 12) a une ouverture de sortie (14, 16) façonnée en pipette ou en buse ayant une dimension maximale entre 1 et 100 µm, préférablement entre 1 et 30 µm;

et en ce que lesdits moyens pour soumettre le liquide à une pression sont des moyens pour soumettre le liquide présent dans le conteneur à au moins une impulsion de pression contrôlée an amplitude et/ou durée.

8. Appareil selon la revendication 7, caractérisé en ce qu'il comprend des moyens pour la connection pneumatique entre ledit conteneur (10), du côté opposé à l'ouverture de sortie, et une source (34) de gaz sous pression, lesdits moyens comprenant une vanne de commande (38) et un ou plusieurs conduits (42) reliant ladite vanne au conteneur, ledit conduit ou conduits étant dimensionnés de sorte à réduire autant que possible le volume de gaz entre l'échantillon liquide dans le conteneur (10) et la vanne de commande (38).

9. Appareil selon la revendication 8, caractérisé en ce qu'il comprend des moyens (36) pour régler la pression entre 1 et 10 atmosphères et des moyens (40) pour contrôler le temps d'ouverture de la vanne entre 1 milliseconde et 1 seconde.

10. Appareil selon la revendication 7, caractérisé en ce que lesdits moyens pour soumettre le liquide à une ou plusieures impulsions de pression comprennent: au moins un transducteur (50, 64) capable de produire une ou plusieures impulsion de pression, à des valeurs de pression élevées et de durée limitée, dans le conteneur d'échantillon (44); une source d'impulsions (54) pour exciter ledit transducteur et des moyens (56, 57) pour régler l'amplitude des impulsions et/ou le nombre des mêmes.

11. Appareil selon la revendication 10, caractérisé en ce que le transducteur est un transducteur piézo-électrique (50) et en ce que ladite source (54) est une source d'impulsions électriques de haute raideur.

12. Appareil selon la revendication 11, caractérisé en ce que ledit conteneur (44) est en verre ou en silice fondue et est entouré, à proximité de son ouverture de sortie, par un transducteur piézo-électrique (50) plongé dans un petit bloc (52) en matériau plastique.

13. Appareil selon la revendication 10, caractérisé en ce que le conteneur (44) a au moins une partie faite de nickel dans la zone contenant l'échantillon liquide; en ce que le transducteur est formé par un appareil magnétostrictif (64) capable d'agir sur ladite partie du conteneur lorsqu'il se trouve dans sa position de travail à l'intérieur d'un siège prévu dans ledit appareil magnétostrictif, et en ce que ledit appareil

comprend des moyens pour recevoir au moins une impulsion de courant ayant une amplitude réglable pour donner lieu à une impulsion de pression dans ladite partie en nickel dudit conteneur.

14. Appareil selon la revendication 13, caractérisé en ce que ladite impulsion a une durée qui dépend de la fréquence de résonance mécanique de l'appareil magnétostrictif et est réglable en amplitude.

15. Emploi d'un appareil selon une des revendications de 7 à 14, dans des systèmes de chromatographie en phase gazeuse à haute résolution avec une colonne capillaire, caractérisé en ce que ledit conteneur (10, 12) a au moins une extrémité ayant une dimension maximale inférieure au diamètre interieur de ladite colonne capillaire où la séparation chromatographique a lieu, et en ce que ledit système de chromatographie en phase gazeuse set pourvu d'un injecteur du type directe en colonne avec des moyens pour contrôler axialement la position du conteneur de sorte que l'extrémité du même pénètr dans l'ouvertur d'entrée d la colonne.

16. Emploi d'un appareil sel n au m ins une des r vendications de 7 à 14, dans des systèms d chr matographie en phase gaz use à haute résolution avec une colonne capillaire, caractérisé en ce que ledit système de chromatographie est pourvu d'un injecteur (70) présentant un dispositif pour l'alignement réciproque et le centrage axial de l'extrémité d'entrée de la colonne de chromatographie (66) et de la sortie du conteneur (10, 72), dans une position axialement espacée jusqu'à une distance de 10 mm au maximum.

17. Emploi selon la revendication 16, caractérisé en ce que ledit système de chromatographie est pourvu de moyens pour coupler l'alimentation de gaz vecteur au cours de l'injection.

18. Emploi selon la revendication 16 ou 17, caractérisé en ce qu'un élément de protection extérieure (74) est associé au moins à la partie terminale du conteneur.

Fig. 1

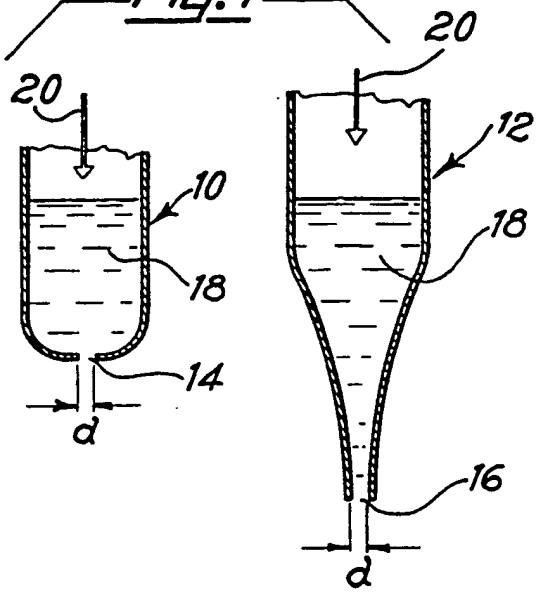

Fig. 2

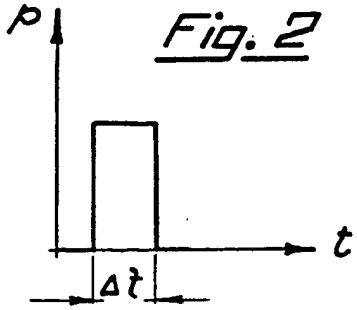

Fig. 3

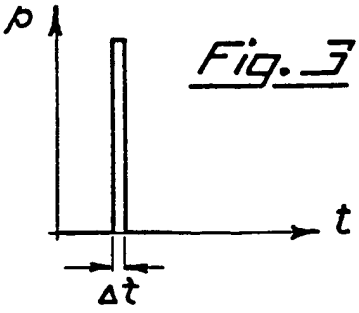

Fig. 4

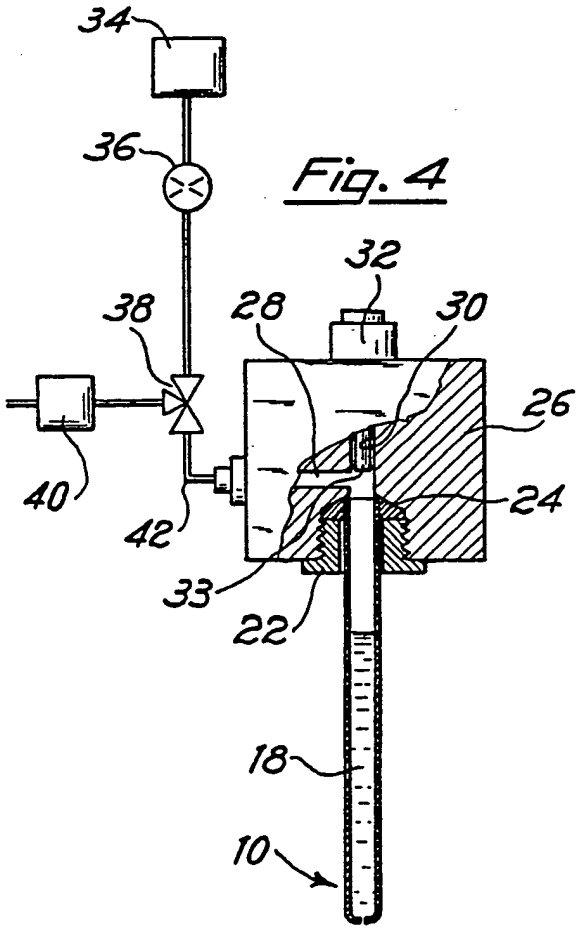

Fig. 5

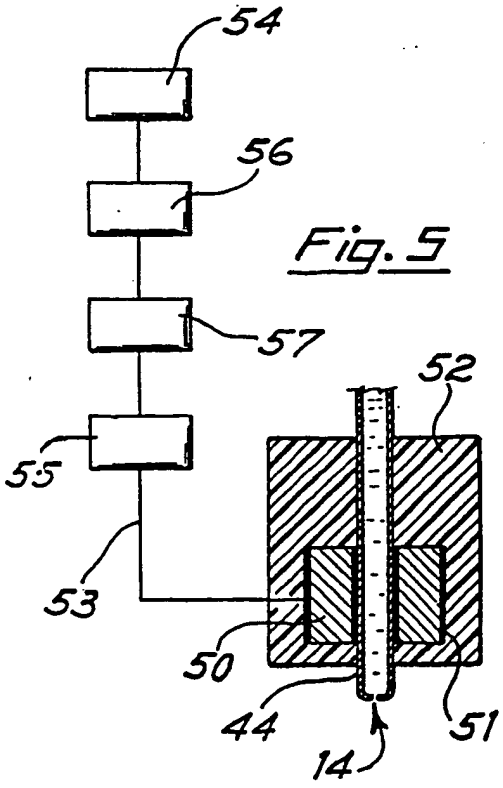

Fig. 6

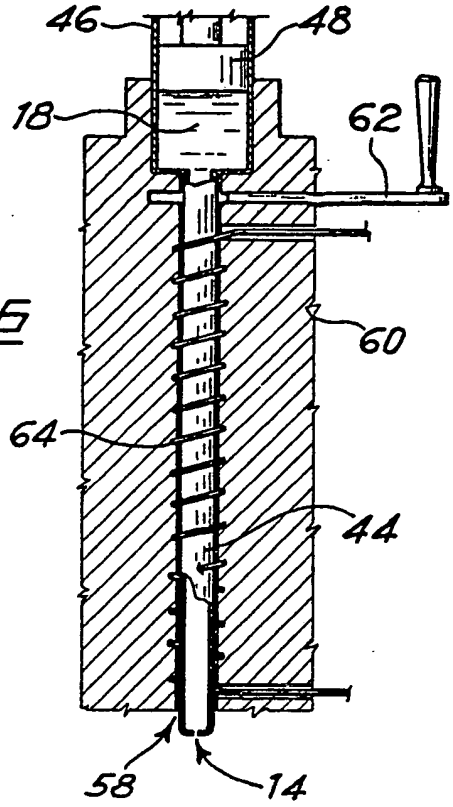

Fig. 7

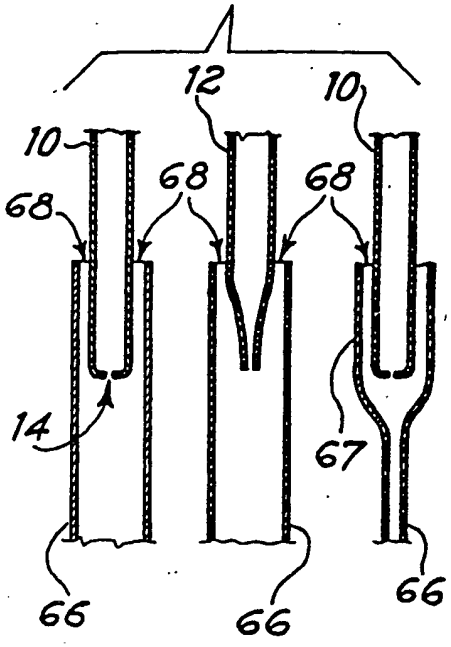

Fig. 8

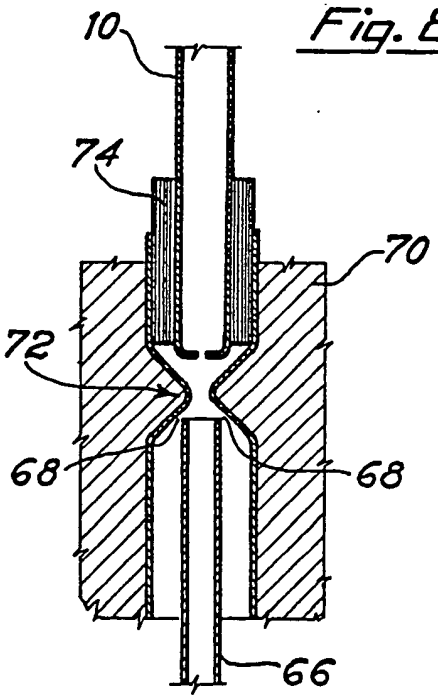

Fig. 9